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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/385,918	08/30/99	HOEKSTRA	M 860098,433
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000500 HM12/1201  
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EXAMINER

ANDRES, J

ART UNIT

PAPER NUMBER

1646

DATE MAILED:

12/01/00

*9*

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

<p align="center"><b>Office Action Summary</b></p>	<p>Application No.</p> <p>09/385,918</p>	<p>Applicant(s)</p> <p>HOEKSTRA ET AL.</p>	
	<p>Examiner</p> <p>Janet L Andres</p>	<p>Art Unit</p> <p>1646</p>	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-54 is/are pending in the application.
- 4a) Of the above claim(s) 11-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☒ Claim(s) 1 is/are objected to.
- 8) ☐ Claims \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

**Attachment(s)**

- |                                                                                              |                                                                              |
|----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| 15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                 | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____   |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)        | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ | 20) <input type="checkbox"/> Other: ____                                     |

### **DETAILED ACTION**

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1646.

#### ***Election/Restrictions***

2. Applicant's election of Group I, claims 1-10, and species election of BMP/SMAD1/SMAD5 in paper no. 8 is acknowledged. Claims 1-10 are pending in this application. Claims 11-54 are withdrawn from consideration as being drawn to a non-elected invention.

#### ***Claim Objections***

3. Claim 1 is objected to as containing language encompassing a non-elected species of invention. Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

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4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
5. Claims 1 and 3-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zhu et al. (Nature, August 12, 1999, Vol. 400, pages 687-693 in view of Husted et al. (U.S. patent 6,087,122, filed July 21, 1999). Zhu et al. teaches a human Smad ubiquitin ligase, hSmurf1, that is a HECT E3 kinase. Zhu et al. further teaches that hSmurf1 interacts with Smads 1 and 5 and enhances turnover (p. 688) and that "Smurf 1 associates specifically with Smad 1 and Smad 5 through interactions between the PY motif in Smad 1 and the WW domains of Smurf 1" (p. 689). Zhu et al. fails to teach a method of screening. Husted et al. teaches human E3 ubiquitin protein ligase biomolecules and teaches that they can be used in screening assays to identify "blockers, antagonists, or inhibitors which bind, emulate substrate, or otherwise inactivate or compete with the biomolecule" (column 14, lines 52-60). Husted et al. further teaches the use of E3 ubiquitin protein ligase, immunogenic fragments, or oligopeptides for screening therapeutic compounds in assays in which the fragment is free or bound and the formation of binding complexes are tested (column 22, lines 1-19) and teaches the use of ELISAs and radiolabelling (figure 1). Husted et al. does not teach Smad 1 or Smad 5 and effects on BMP activity or the assays based on the binding of Smads to HECT E3 ubiquitin ligase. However, it would have been obvious to one of ordinary skill in the art to combine the teachings of Zhu et al with those of Husted et al. to use the interaction of Smad 1 or Smad 5 and a HECT E3 ubiquitin protein ligase to screen for effectors of BMP function. One of ordinary skill would be motivated to do so because Zhu et al. teaches that "targeted ubiquitination of SMADS may serve to control both embryonic development and a wide variety of cellular responses to TGF-beta signals (p. 687)".

*Claim Rejections - 35 USC § 112*

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6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods using a HECT E3 ubiquitin ligase domain, does not reasonably provide enablement for methods using variants of either such a domain or of a polypeptide comprising such a domain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicant has described several WW domains, but has not described the structural characteristics or conserved regions of these sequences so that one of skill in the art would be able to predict which variants, if any, would function as claimed. Thus one of skill in the art would require additional guidance, such as information as to what structural features would result in SMAD binding, to determine what other polypeptides would predictably function as claimed. Without such guidance, it would require undue experimentation for one of skill to practice the invention commensurate with the scope of the claims.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

These claims are drawn to methods using a "HECT E3 ubiquitin ligase WW domain or variant thereof" and a "SMAD PY motif". Use of these terms is indefinite because they only

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describe the protein of interest by an arbitrary name. The claims should refer to a sequence presented in the sequence listing. While the name itself may have some notion of the activity of the protein, there is nothing in the claim that distinctly identifies the protein. Applicant should particularly point out definitive characteristics associated with the protein. Describing biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly identify what the protein is. In addition, "thereof" is indefinite. As written, the variation could be either in the WW domain, or in the polypeptide comprising this domain, and thus not necessarily within the WW domain. The claims are further indefinite in the recitation of "substantially diminished". One of skill in the art would not be able to determine what level of diminution would be considered "substantial".

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Andres, Ph.D., whose telephone number is (703) 305-0557. The examiner can normally be reached on Monday through Friday from 8:00 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached at (703) 308-6564. The fax phone number for this group is (703) 305-3014 or (703) 308-4242.

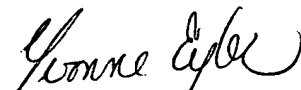
Communications via internet mail regarding this application, other than those under U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

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All Internet email communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Janet Andres, Ph.D.  
November 30, 2000

  
YVONNE EYLER, PH.D.  
PRIMARY EXAMINER